

**What is claimed is:**

1. An isolated nucleic acid, which encodes a polypeptide having an amino acid sequence that is at least 75% identical to the amino acid sequence for mature human AL-2 shown in Figure 1A-1B or Figure 2A-2B.

5 2. The isolated nucleic acid according to claim 1, which encodes a polypeptide having an amino acid sequence that is at least 85% identical to the amino acid sequence for mature human AL-2 shown in Figure 1A-1B or Figure 2A-2B.

3. The isolated nucleic acid of claim 2, comprising a nucleotide sequence encoding the amino acid sequence shown in Figure 1A-1B for mature AL-21.

4. The isolated nucleic acid of claim 2, comprising a nucleotide sequence encoding the amino acid sequence shown in Figure 2A-2B for mature AL-2s.

5. The isolated nucleic acid of claim 2, which encodes a polypeptide having an amino acid sequence that is at least 75% homologous to the amino acid sequence of the extracellular domain of AL-2 shown in Figure 1A-1B.

15 6. The isolated nucleic acid of claim 5, which encodes a polypeptide having the amino acid sequence of the extracellular domain shown in Figure 1A-1B for AL-2.

7. The isolated nucleic acid of claim 1, wherein AL-2 is joined to an immunoglobulin.

8. The isolated nucleic acid of claim 7, which encodes AL-2-IgG.

9. The isolated nucleic acid of claim 1, wherein AL-2 is fused to a tag polypeptide.

20 10. The isolated nucleic acid of claim 1, which hybridizes to DNA encoding mature human AL-21 of Figure 1A-1B or mature human AL-2s of Figure 2A-2B under stringent conditions, and which encodes a polypeptide that is antigenically cross-reactive to mature human AL-2s or AL-21.

11. An expression vector comprising the nucleotide sequence of claim 1 operably linked to a promoter.

25 12. The expression vector of claim 11, wherein the nucleotide sequence encodes the amino acid sequence for mature AL-2 shown in Figure 1A-1B or Figure 2A-2B.

13. The expression vector of claim 12, wherein the nucleotide sequence encoding the amino acid sequence for mature AL-2 is that shown in Figure 1A-1B or Figure 2A-2B.

14. A host cell transformed with the expression vector of claim 11.

30 15. The host cell of claim 14, wherein the nucleotide sequence encodes the amino acid sequence for mature AL-2 shown in Figure 1A-1B or Figure 2A-2B.

16. A method of using the host cell of claim 14, which method comprises culturing the host cell under conditions that allow replication of the expression vector.

67 83 68

Sub B7  
17. A process which comprises transforming a host cell with an expression vector capable, in the host cell transformed with the vector, of expressing a nucleotide sequence that encodes a polypeptide comprising the amino acid sequence shown in Figure 1A-1B or Figure 2A-2B for mature AL-2, and ~~culturing the transformed host cell under conditions such that the AL-2 polypeptide is synthesized~~

5 18. An isolated polypeptide having an amino acid sequence that is at least 75% homologous to the mature human AL-2 amino acid sequence shown in Figure 1A-1B or Figure 2A-2B.

19. The isolated polypeptide of claim 18 having an amino acid sequence that is at least 85% homologous to the mature human AL-2 amino acid sequence shown in Figure 1A-1B or Figure 2A-2B.

10 20. The isolated polypeptide of claim 19 having the mature human AL-2 amino acid sequence shown in Figure 1A-1B or Figure 2A-2B.

21. The isolated polypeptide of claim 18 having an amino acid sequence that is at least 75% homologous to the amino acid sequence of the extracellular domain shown in Figure 1A-1B for mature human AL-2.

15 22. The isolated polypeptide of claim 21 having the amino acid sequence of the extracellular domain shown in Figure 1A-1B for AL-2.

23. The isolated polypeptide of claim 18, wherein AL-2 is joined to an immunoglobulin.

24. The polypeptide of claim 23, wherein the AL-2 extracellular domain is joined to an immunoglobulin constant domain.

20 25. The polypeptide of claim 24, wherein the constant domain is that of an immunoglobulin heavy chain.

26. The polypeptide of claim 23 that is AL-2-IgG.

27. The polypeptide of claim 18, wherein AL-2 is fused to a tag polypeptide.

28. A pharmaceutical composition comprising the polypeptide of claim 18 and a physiologically acceptable carrier.

25 29. An antibody that specifically binds to a polypeptide having the amino acid sequence shown in Figure 1A-1B for mature AL-2.

30. The antibody of claim 29 that is a monoclonal antibody.

31. A method for activating a tyrosine kinase domain of an AL-2-binding Eph-family receptor, comprising contacting an extracellular domain of the receptor with the AL-2 of claim 1.

30 32. A method of treating a neurologic disease or disorder in a mammal, comprising administering to the mammal a therapeutically effective amount of the composition of claim 28.

33. The method of claim 32 wherein the neurologic disease or disorder is trauma-induced, surgery-induced, stroke-induced, ischemia-induced, infection-induced, metabolic disease-related, nutritional

deficiency-induced, malignancy-induced, neurotoxicity, Alzheimer's disease, amyotrophic lateral sclerosis, Bell's palsy, spinal muscular atrophy or paralysis, Parkinson's disease, epilepsy, multiple sclerosis, Huntington's chorea, Down's Syndrome, nerve deafness, Meniere's disease, post-polio syndrome, Charcot-Marie-Tooth disease, Refsum's disease, Abetalipoproteinemia, Tangier disease, Krabbe's disease,

5 Metachromatic leukodystrophy, Fabry's disease, and Dejerine-Sottas syndrome.

34. The method of claim 32 that further comprises administering a therapeutically effective amount of a second neurotrophic factor.

35. A method for accelerating the neovascularization of a wound, comprising applying to the wound an angiogenically effective amount of the composition of claim 28.

10 36. A method of modulating angiogenesis associated with a disease condition in a mammal, comprising administering to the mammal an angiogenically-modulating amount of an AL-2 antagonist.

37. The method of claim 36, wherein the angiogenesis-associated disease condition is rheumatoid arthritis or tumor formation.

15 38. A method of diagnosing a neurologic disease or disorder, comprising contacting nucleic acid of a sample with a second nucleic acid comprising at least 10 nucleotides of the nucleotide sequence shown in Figures 1A-1B or 2A-2B under conditions that allow hybridization of complementary nucleotide sequences, and detecting any hybridization that occurs.

39. The method of claim 38, further comprising amplifying the sample nucleic acid to which the second nucleic acid hybridizes.

Add  
B8

Add  
C7

Add  
D1